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MERCK AND CO., INC			MURRAY, JEFFREY H	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/537,187	Applicant(s) PARMEE ET AL.
	Examiner JEFFREY H. MURRAY	Art Unit 1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
 - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
 - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED. (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 19 December 2007.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-21 is/are pending in the application.
- 4a) Of the above claim(s) 21 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1-18 and 20 is/are rejected.
- 7) Claim(s) 19 is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) Notice of References Cited (PTO-892)
 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
 3) Information Disclosure Statement(s) (PTO-166/08)
 Paper No(s)/Mail Date _____
- 4) Interview Summary (PTO-413)
 Paper No(s)/Mail Date _____
- 5) Notice of Informal Patent Application
 6) Other: _____

DETAILED ACTION

Status of Claims

1. Claims 1-18 and 20 are rejected. Claim 19 is objected. Claim 21 is withdrawn.
2. Claims 1-21 are pending in this application. Claims 4 and 5 have been cancelled. Claim 21 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. This action is in response to the applicants' amendment after a non-final and reply filed on December 19, 2007.

Status of Objections

3. The specification was objected to as not properly indicating trademarks. The objection to the specification is hereby withdrawn.

Status of Rejections

4. Claims 1-18 and 20 are rejected under 35 U.S.C. 112, first paragraph as failing to comply with the enablement requirement. The rejection of Claims 1-18 and 20 is withdrawn in part and upheld in part in view of applicants' arguments and amendments. Applicants have stated that in order to advance prosecution they have amended the claims 1, 6, 7, and 16-19 and cancelled claims 4 and 5. The rejection of claims 4 and 5 are now moot. The rejection of Claims 1-3, 6-18 and 20 are still upheld. The rejection is stated below. Please refer to this section for a detailed explanation of the rejection.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior office action.

Maintained/New Rejections

Claim Rejections - 35 USC § 112, 1st paragraph

5. Claims 1-3, 6-18 and 20 are still rejected under 35 U.S.C. 112, first paragraph for the reasons of record, as the applicants arguments have not been found persuasive. The specification, while being enabling for compounds, compositions, or pharmaceutically acceptable salts where R¹ is an alkyl, cycloalkyl, or optionally substituted phenyl or benzyl and Y being a 4-alkylcyclohexyl group does not reasonably provide enablement for all other compounds with residue groups other than those described above listed within the claims or any solvates. The specification does not

enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

6. The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art without undue experimentation. (*United States v. Teletronics Inc.*, 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is needed is not based on a single factor, but rather a conclusion reached by weighing many factors (See *Ex parte Forman* 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988)).

These factors include the following:

1) *Amount of guidance provided by Applicant.* While the Applicant has demonstrated within the application how to make numerous compounds, only compounds with R¹ as an alkyl, cycloalkyl, or optionally substituted phenyl or benzyl and Y as a 4-alkylcyclohexyl group. Claim 1 is massive, and only a small fraction of these "potential" compounds are discussed. Applicant has provided no guidance, examples, or provided any chemical or biological data and/or testing results of any compounds, pharmaceutically acceptable salts, or solvates other than those described above with a specific R¹ and Y moieties in the current application.

2) *Unpredictability in the art.* It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved", and physiological activity is generally considered to be an unpredictable factor. (USPQ 18, 24 (CCPA 1970). See *In re Fisher*, 427 F.2d 833, 839, 166.

Chemistry is unpredictable. See *In Re Marzocchi and Horton* 169 USPQ at 367

paragraph 3:

"Most non-chemists would probably be horrified if they were to learn how many attempted syntheses fail, and how inefficient research chemists are. The ratio of successful to unsuccessful chemical experiments in a normal research laboratory is far below unity, and synthetic research chemists, in the same way as most scientists, spend most of their time working out what went wrong, and why. Despite the many pitfalls lurking in organic synthesis, most organic chemistry textbooks and research articles do give the impression that organic reactions just proceed smoothly and that the total synthesis of complex natural products, for instance, is maybe a labor-intensive but otherwise undemanding task. In fact, most syntheses of structurally complex natural products are the result of several years of hard work by a team of chemists, with almost every step requiring careful optimization. The final synthesis usually looks quite different from that originally planned, because of unexpected difficulties encountered in the initially chosen synthetic sequence. Only the seasoned practitioner who has experienced for himself the many failures and frustrations which the development (sometimes even the repetition) of a synthesis usually implies will be able to appraise such workChemists tend not to publish negative results, because these are, as opposed to positive results, never definite (and far too copious) " Dorwald F. A. *Side Reactions in Organic Synthesis*, 2005, Wiley: VCH, Weinheim pg. IX of Preface.

The scope of "solvate" is not adequately enabled or defined. Applicants provide no guidance as how the compounds are made more active *in vivo*. Solvates cannot be predicted and therefore are not capable of being claimed if the applicant cannot properly enable a particular solvate.

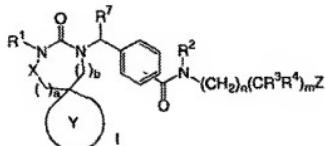
"Predicting the formation of solvates or hydrates of a compound and the number of molecules of water or solvent incorporated into the crystal lattice of a compound is complex and difficult. Each solid compound responds uniquely to the possible formation of solvates or hydrates and hence generalizations cannot be made for a series of related compounds. Certain molecular shapes and features favor the formation of crystals without solvent; these compounds tend to be stabilized by efficient packing of molecules in the crystal lattice, whereas other crystal forms are more stable in the presence of water and/or solvents. There may be too many possibilities so that no computer programs are currently available for

predicting the crystal structures of hydrates and solvates. (Vippagunta et al. Advanced Drug Delivery Reviews 48 (2001) 3-26.

3) *Number of working examples.* The compound core depicted with specific substituents represent a narrow subgenus for which applicant has provided sufficient guidance to make and use; however, this disclosure is not sufficient to allow extrapolation of the limited examples to enable the scope of the compounds instantly claimed or preventive agents. Applicant has provided no working examples of any compounds where the R¹ or Y moieties is not that previously defined above in the present application.

Within the specification, "specific operative embodiments or examples of the invention must be set forth. Examples and description should be of sufficient scope as to justify the scope of the claims. *Markush* claims must be provided with support in the disclosure for each member of the *Markush* group. Where the constitution and formula of a chemical compound is stated only as a probability or speculation, the disclosure is not sufficient to support claims identifying the compound by such composition or formula." See MPEP 608.01(p).

4) *Scope of the claims.* The scope of the claims involve all of the tens of thousands of compounds of general formula I:



Wherein Y is a cycloalkyl ring; X is a -CH₂-; and, a or b=1. Thus, the scope of claims is very broad.

5) *Nature of the invention.* The nature of this invention relates generally to spirocyclic urea derivatives, compositions containing such compounds, and their methods of treating type 2 diabetes mellitus.

6) *Level of skill in the art.* The artisan using Applicants invention would be a chemist with a Ph.D. degree, and having several years of bench experience.

MPEP §2164.01 (a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here that Applicant is not enabled for making most of the compounds or compositions mentioned in the current application.

Allowable Subject Matter

7. Claim 19 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim 19 would be allowable because the claim specifically contains compounds that are not defined in any of the prior art. The limitation not seen in the prior art is the presence of a spirocycloalkyl group attached to the tetrahydropyrimidin-2(1H)-one ring,

in particular a 4-alkylcyclohexyl group present to make substituted 1,3-diazaspiro[5.5]-undecan-2-one derivatives.

Conclusion

8. Claims 1-3, 6-18 and 20 are rejected.
9. Claim 19 is objected.
10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey H. Murray whose telephone number is 571-272-9023. The examiner can normally be reached on Mon.-Thurs. 7:30-6pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson can be reached at 571-272-0661. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jeffrey H Murray/
Patent Examiner
Art Unit 1624

/James O. Wilson/
Supervisory Patent Examiner
Art Unit 1624